CHO Cell Perfusion Bioreactor Model

1. Viable Cell Growth (Discrete Form)

$$X_v(t + \Delta t) = X_v(t) + \Delta t \cdot [\mu(t) \cdot X_v(t) - k_d \cdot X_v(t)] \tag{1}$$

2. Dead Cell Accumulation

$$X_d(t + \Delta t) = X_d(t) + \Delta t \cdot [k_d \cdot X_v(t) - D(t) \cdot X_d(t)] \tag{2}$$

3. Specific Growth Rate (Monod Kinetics + Inhibition + Density Limitation)

$$\mu(t) = \mu_{\max} \cdot \frac{G(t)}{G(t) + K_G} \cdot \frac{Q(t)}{Q(t) + K_Q} \cdot \frac{DO}{DO + K_{DO}} \cdot \left(1 - \frac{X_v(t)}{X_{v,\max}}\right) \cdot \exp\left(-\alpha_L \cdot L(t) - \alpha_A \cdot A(t) - \alpha_{\text{pH}} \cdot |pH - pH_{\text{opt}}| - \alpha_T \cdot |T - \right. \tag{3}$$

where:

- $X_v(t)$ is the viable cell density at time t [cells/mL]
- $X_{v,\max}$ is the maximum viable cell density [cells/mL] beyond which no further growth occurs

4. Substrate Dynamics

4.1 Glucose

$$G(t + \Delta t) = G(t) + \Delta t \cdot [-q_G \cdot X_v(t) + D(t) \cdot (G_{\text{in}} - G(t))] \tag{4}$$

4.2 Glutamine

$$Q(t + \Delta t) = Q(t) + \Delta t \cdot [-q_Q \cdot X_v(t) + D(t) \cdot (Q_{\text{in}} - Q(t))] \tag{5}$$

5. Byproduct Dynamics

5.1 Lactate

$$L(t + \Delta t) = L(t) + \Delta t \cdot \left[Y_{L/G} \cdot q_G \cdot X_v(t) - D(t) \cdot L(t)\right] \tag{6}$$

5.2 Ammonia

$$A(t + \Delta t) = A(t) + \Delta t \cdot \left[Y_{A/Q} \cdot q_Q \cdot X_v(t) - D(t) \cdot A(t)\right] \tag{7}$$

6. Product Formation

$$P(t + \Delta t) = P(t) + \Delta t \cdot [q_P \cdot X_v(t) - D(t) \cdot P(t)] \tag{8}$$

7. Perfusion Dilution Rate

$$D(t) = \begin{cases} D_{\text{pump}}, & \text{if } G(t) < G_{\min} \\ D_{\text{base}}, & \text{otherwise} \end{cases} \tag{9}$$

8. Total Biomass

$$\text{Total Biomass} = (X_v + X_d) \cdot V \tag{10}$$

Model Parameters

Symbol	Description	Unit	Value
$\mu_{\max}$	Max specific growth rate	1/h	0.04
k_d	Cell death rate	1/h	0.005
q_G	Glucose uptake rate	g/(cells·h)	0.03
q_Q	Glutamine uptake rate	g/(cells·h)	0.02
q_P	Product formation rate	g/(cells·h)	0.001
$Y_{L/G}$	Lactate yield per glucose	g/g	0.9
$Y_{A/Q}$	Ammonia yield per glutamine	g/g	1.2
K_G	Monod constant (glucose)	g/L	0.5
K_Q	Monod constant (glutamine)	g/L	0.3
K_{DO}	Monod constant (oxygen)	%	5
DO	Dissolved oxygen level	%	100
$X_{v,\max}$	Max viable cell density (growth-limiting threshold)	cells/mL	20
α_L	Lactate inhibition coefficient	1/g	0.02
α_A	Ammonia inhibition coefficient	1/g	0.03
α_{pH}	pH inhibition coefficient	–	0.05
α_T	Temperature inhibition coefficient	–	0.04
pH	Culture pH	–	7.2
pH_{opt}	Optimal pH	–	7.2
T	Culture temperature	°C	37
T_{opt}	Optimal temperature	°C	37
D_{pump}	High perfusion rate	1/h	0.1
D_{base}	Base dilution rate	1/h	0.001
$G_{\min}$	Glucose threshold for perfusion	g/L	4.0
G_{in}	Inlet glucose concentration	g/L	8.0
Q_{in}	Inlet glutamine concentration	g/L	5.0
V	Reactor volume	L	1.0–2.0
Δt	Time step	h	0.1